REMARKS/ARGUMENTS

The specification is amended to include continuity data on the first paragraph to comply with 37 CFR 1.78(a)(2). The statement of continuity includes references to the Canadian application as well as the PCT application pursuant to which the pending US National Phase application of which the present application is a divisional, was filed. The previous Abstract is canceled and replaced with a new abstract that is being submitted on a separate sheet of paper, in compliance with 37 C.F.R. 1.72. Claims 65-68 and 68-77 remain pending in this application. Applicants wish to tank the Examiner for the indication of allowable subject matter in claims 66, 68 and 70-73. Claims 65, 69, 74, 75, 76 and 77 are amended above.

The Examiner has objected to the specification under 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Claims 65, 66 and 68-77 are amended to dispense with the terms "reference solution" and to recite "hypothetical solution", antecedent basis for which is provided in the specification. Withdrawal of the objection is respectfully requested. The Examiner has also objected to claims 69 and 74-77 under 37 CFR 1.75(a) for lack of antecedents in respect of certain terms. Claims 69, 74 and 75 have been amended above to overcome these objections.

Claim 5 stands rejected under 35 U.S.C. 102(b) as being anticipated by "Checking pH without an Electrode" (Sykes et al.). Applicants respectfully traverse this rejection for at least the following reasons. As best understood, Sykes et al. sought to find a way to check the pH of a protein sample internally, not a process for producing a representation of a reference spectrum, as claimed by the present applicants. At lines 4-5 Sykes et al. state: "This prompted us to find a way to check the pH of the sample internally". Thus, by observing chemical shifts, Sykes et al. sought to determine pH, not use it to produce a reference spectrum as required by claim 65.

Sykes et al. discovered two peaks in the amide region of a protein ^{1}H NMR spectrum, whose resonance frequencies are pH dependent. Sykes et al. fit the observed chemical shifts to his equation 1 to determine the chemical shift of the conjugate acid and the chemical shift of the conjugate base over a range of pH values and determined the values 8.66 and 7.76 respectively. They then used these values in his equation 2 to get pH of the sample. Sykes et al. describe a

macro for use in Varian's VNMR processing software to check the pH in 1D ^{1}H NMR spectra of his protein samples.

There is no disclosure in Sykes of a "computer-implemented process for producing a representation of a reference spectrum for a hypothetical solution having a first pH condition, for use in determining the composition of a test sample", as recited in claim 65. Furthermore, Sykes et al. fail to disclose "producing a position value for at least one peak of the reference spectrum in response to a measured pH condition of the test sample, and a property of at least one peak in a base reference spectrum for the hypothetical solution...." as recited in claim 65. Rather, Sykes et al. sought to find a pH condition of the test sample based on observed chemical shifts. In addition, Sykes et al. provide no disclosure to use a base reference spectrum associated with a pH condition of the hypothetical solution that is different from said measured condition, as required by claim 65. Sykes et al. provide no disclosure to produce a reference spectrum for a hypothetical solution at the measured pH from a base reference spectrum associated with the hypothetical solution having a pH different from said measured pH. Therefore, applicants respectfully submit that Sykes et al. fail to teach or suggest claim 65. Claim 65 and its dependent claims 66, and 68-73 are thus allowable over Sykes.

Claims 74-77 are rejected under 35 USC 103(a) as being unpatentable over "Checking pH without an Electrode" (Sykes et al.) The Examiner asserts that Sykes et al. disclose a set of codes "...to produce a position value for at least one peak of the reference spectrum..." Applicants respectfully submit that as stated above in connection with claim 65, the macro provided by Sykes et al. and its use with Varian's VNMR processing software are stated to be specifically for checking the pH in 1D ^{1}H NMR spectra of protein samples, not for producing a position value as claimed by the present applicant. Furthermore, there is nothing to suggest that a position value for at least one peak of the reference spectrum should be produced in response to a measured pH condition of the test sample and a property of at least one peak in a base reference spectrum for the hypothetical solution, as required by claims 74-77. Consequently, Sykes et al. provide no motivation or suggestion to arrive at the applicant's claimed invention. Claim 74 is further

allowable over Sykes for these additional reasons. Claims 75 and 76 are allowable for at least the same reasons as is claim 74.

As for claim 77, Sykes et al. fail to disclose or suggest producing a representation of a reference spectrum for a hypothetical solution having a first pH condition, for use in determining the composition of a test sample. Rather, Sykes et al. disclose checking the pH of a protein sample. Claim 77 further recites means for receiving a measured pH condition value representing a pH condition of the test sample. The Examiner states that this is disclosed on page 479-11, but the context of this disclosure suggests that a pH electrode was used to measure pH; Sykes et al. sought to obviate the need for such measurement, or to provide a secondary means for checking pH of the sample. Thus, Sykes et al. fail to disclose or suggest any use of a measurement of pH, as Sykes seeks only a way of making the measurement.

Claim 77 further recites means for receiving a representation of a position value of at least one peak in a base reference spectrum for the hypothetical solution and means for producing a position value for at least one peak of the reference spectrum in response to said measured pH condition value of the test sample, and the position value of said at least one peak in said base reference spectrum, the base reference spectrum being associated with a pH condition of the hypothetical solution that is different from said measured pH condition.

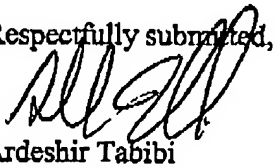
On page 479-11, Sykes provides background in support of the use of his macro which appears on page 479-12. This background provides a theory behind pH dependent chemical shifts to support only one application thereof – checking pH of the sample. Sykes et al. provide no disclosure or suggestion to employ such theory or other theories to provide a process or apparatus for producing a representation of a reference spectrum including means for producing a position value for at least one peak of the reference spectrum as claimed. In other words, Sykes et al. fail to disclose or suggest or provide any motivation to employ the specific application of knowledge of pH dependent chemical shifts to provide a method or apparatus for producing a representation of a reference spectrum, as claimed in the instant application. Claim 77 is thus allowable for these additional reasons.

Claim 69 is rejected under 35 USC 103(a) as being unpatentable over "Checking pH without an Electrode" (Sykes et al.) in view of Otvos (5,343,389). Claim 69 is dependent upon claim 65 and is thus allowable for at least the same reasons as is claim 69.

The Examiner however, relies on Otvos for the additional limitation of claim 69 which further adds to claim 65 the limitation that a "pre-defined record specifying peaks in said reference spectrum and wherein producing said position value comprises adjusting a position value in said pre-defined record, said position value in said pre-defined record being said position value of said at least one peak". Thus, it specifies a source for the at least one peak of the reference spectrum in the context of the use of measured pH to "adjust " a base reference spectrum for a hypothetical reference solution at a first pH to produce a reference spectrum for the hypothetical solution at the measured pH. Neither Sykes et al, nor Otvos, whether taken alone, or in combination teach or suggest accessing a pre-defined record specifying peaks in a reference spectrum in this context. Claim 69 is thus allowable for these additional reasons.

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance and an action to that end is respectfully requested. If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at (650) 326-2400.

Respectfully submitted,



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APPENDIX

ABSTRACT

A computer implemented process for producing a representation of a reference spectrum for a hypothetical solution having a first pH condition, for use in determining the composition of a test sample, is disclosed. The process involves producing a position value for at least one peak of the reference spectrum in response to a measured pH condition of the test sample and a property of at least one peak in a base reference spectrum for the hypothetical solution, the base reference spectrum being associated with a pH condition of the hypothetical solution that is different from said measured pH condition.